

-25-  
REMARKS

Claims 1 to 33, 35, 38 to 40, and 71 to 97, 112 to 132, and 134 are in the application. With this amendment, claim 133 has been cancelled. Claims 1, 11-17, 19, 25, 26, 28, 31, 33, 35, 38, 72, 73, 76, 78, 80, 84, 86, 88-92, 112-116, 118, 122, 123, 125, 128, 130, 132 and 134 have been amended. Support for the amendments can be found throughout the specification, for example: page 24 line 33 to page 25, line 2; page 28, lines 4 to 34, and page 29 lines 7 to 9; the claims as originally filed; and in the working examples. No new matter is believed added. Applicants reserve their right to file divisional or continuation applications on cancelled or deleted subject matter.

**Rejection of Claims under 35 USC §112**

I. Rejection of Claims 1-33, 35, 38-40, 71-97 and 112-134 under 35 USC §112, first paragraph

The Examiner has rejected the claims listed above for “failing to comply with the written description requirement... While the present specification at page 28 discloses dissolution modifying excipients can be mixtures with each other, it appears that nowhere in the present specification provides support for newly added limitations ‘first and second dissolution modifying excipients’”. Applicants respectfully traverse this rejection.

As the Examiner noted, the specification does support combinations of dissolution modifying excipients. To clarify this aspect of the present invention, the claims have been amended to encompass a combination of dissolution modifying excipients, with at least one dissolution modifying excipient, and at least one other dissolution modifying excipient. The Examiner will certainly agree that to achieve a combination of dissolution modifying excipients as recited in the specification, there will inherently be at least one dissolution modifying excipient, and at least one other dissolution modifying excipient, present in the composition. The specification fully supports this amendment, and therefore withdrawal of the rejection of these claims under 35 USC §112, first paragraph, is respectfully requested.

II. Rejection of Claims 15, 19, 31, 35, 72, 86 and 89 under 35 USC §112, second paragraph

The Examiner rejected claims 15, 19, 86, and 89 based on the recitation of “the dissolution modifying excipient” as being unclear whether the recitation is referring to the “first”, “second” or both of the dissolution modifying agents in claim 1. These claims, and claim 1, have been amended to clarify this aspect of the present invention. As such, withdrawal of this rejection is respectfully requested.

The Examiner rejected claim 31 for “failing to further limit the subject matter of claim 1.” Claim 1 has now been amended to remove formulations not containing a lubricant, and that now fully encompass the range of lubricants recited in claim 31. Withdrawal of the rejection of claim 31 on this basis is respectfully requested.

The recitation of “low substituted hydroxypropyl cellulose” in claim 31 was considered by the Examiner to lack antecedent basis, and was unclear to the Examiner as to which dissolution modifying excipient this recitation was referring. Claim 31 has been amended to recite “low molecular weight” hydroxypropyl cellulose, which is described on page 28 of the specification. Claim 1 has been amended to clarify the combination of dissolution modifying excipients. As a result, the withdrawal of the rejection of claim 31 under 35 USC §112, second paragraph is respectfully requested.

The Examiner rejected claim 35 for “failing to further limit the subject matter of claim 1”, since this claim recites 5% stearyl alcohol, which falls outside the range of the lubricant recited in claim 1. Claim 1 has been amended to fully encompass the range of lubricants recited in claim 35, and withdrawal of the rejection of claim 35 on this basis is respectfully requested. Claim 35 has also been corrected to properly recite the levels of the components in formulation 11. The Applicants appreciate the Examiner’s thorough review of the format of the claims.

The Examiner rejected claims 35 and 72 as being indefinite, for reciting a “broad range or limitation with a narrow range or limitation that falls within the broad range or limitation (within the same claim)”. Claims 35 and 72 have been amended to delete recitation of “example” of formulations.

Therefore, these claims are believed to no longer be indefinite, and withdrawal of this rejection is respectfully requested.

### **Rejection of Claims under 35 USC §103**

#### I. Rejection of Claims 4, 5, 15, 17, 19, 76-78, 89-92 under 35 USC §103(a) as being unpatentable over Petereit (US Pub. No. 2002/0160042) in view of Hatano (US 6,309,666)

In the Office Action dated June 24, 2008, the Examiner maintained the rejections under 35 USC §103(a). With regard to Petereit, the Examiner, in the 9/20/07 Office Action, stated that Petereit "...teaches injection-molded capsules comprising methacrylate copolymers and other components, such as a release agent, a plasticizer, additives or auxiliaries, pharmaceutical agents, and other polymers or copolymers." The Examiner then stated that Petereit "does not teach the inclusion of additives such as lactose and mannitol or the inclusion of surfactants such as sodium dodecyl sulfate." The Examiner then cited Hatano "solely for the teaching of excipients such as lactose in a capsule shell" (6/24/08 Office Action.)

The Examiner concluded that "(a)s the two references are drawn to enteric compositions, they are clearly within the same field of endeavor. Therefore one of ordinary skill in the art would have a reasonable expectation of success in combining the references." (9/20/07 Office Action.)

The presently amended claims, however, are directed to a capsule shell composition and a linker composition which are **substantially pH independent**.

Nothing in either the Petereit or the Hatano reference teaches, suggests, motivates, or provides any reason, or in fact even remotely enables, the substantially pH independent composition of the present invention which make of the capsule shell and linker as claimed herein.

The Examiner characterized both the Petereit and the Hatano references as relating to enteric compositions. “Enteric” relates to the small intestine, which has a pH ranging from approximately neutral to basic. Clearly, enteric compositions designed to be soluble in the small intestine are not soluble in the low pH gastric environment. This fact is exemplified in each of the Petereit and Hatano references.

Petereit explicitly states that the polymers described therein are “neutral or anionic (meth)acrylate copolymers” (para. 0004). Petereit then goes on to recite numerous (meth)acrylate copolymers, each of which is anionic or neutral (see para. 0032-0038), which is entirely consistent with the Examiner’s characterization of Petereit relating to enteric compositions. Finally, in Example 1 of Petereit, a “Moulding Soluble in Intestinal Fluid” is prepared.

There is no teaching, suggestion, motivation or reason provided in Petereit for making a copolymer-containing capsule shell and linker compositions that are substantially pH independent, as is currently claimed. This is supported in the specification on page 24, lines 33-36 and page 25, lines 1-2. This unexpected achievement has been made by the particular and novel blending of components. This novel blend of excipients is not described, nor suggested by the cited art herein.

As noted above, the Examiner has also characterized Hatano as drawn to enteric compositions, which by definition are not pH independent. In fact, the use of methacrylate co-polymers and acrylic co-polymers in Hatano as described in column 5, line 42 to column 6, line 23 is to create a low pH gastric soluble film **on top of** the hard capsule shell, and an “enteric coating” **on top of** the low pH film layer, with the enteric coating being soluble in a medium having a pH greater than 5 (col. 5, lines 60-64). Therefore, **Hatano is clearly directed to pH dependent compositions**, and combines the pH dependencies to achieve the “enteric composition” described by the Examiner.

There is no teaching, suggestion, motivation or reason for one of ordinary skill in the art to use the teachings of Petereit and Hatano to result in a substantially pH independent

composition as in the present invention. Hatano does not make up for the deficiencies of Petereit with respect to changing the pH dependency of the compositions described in those references, and in fact further exemplifies the unexpectedness of the presently claimed invention, since Hatano utilizes **two separate coatings, each having a different pH solubility** in order to provide the desired release profile. Prior to the present invention, it was not believed possible to prepare a pH-independent **capsule shell or linker itself** using the copolymers as recited in the presently amended claims. Therefore, the claimed invention is not prima facie obvious, and withdrawal of the rejection of these claims over Petereit in view of Hatano under 35 USC §103(a) is respectfully requested.

II. Rejection of Claims 6, 79 and 80 under 35 USC §103(a) over Petereit in view of the Handbook of Pharmaceutical Excipients (hereinafter, "Handbook")

The Examiner maintained the rejection of these claims, stating that the Handbook was "...cited for the teaching of using lubricant and surfactant in a capsule shell...". As discussed previously, Petereit is not directed to and does not teach, suggest or provide any reason for a pH independent capsule shell or linker composition, and the Handbook fails to compensate for this fundamental deficiency in Petereit. These claims, as amended, are not prima facie obvious, and withdrawal of the rejection of these claims over Petereit in view of the Handbook under 35 USC §103(a) is respectfully requested.

II. Rejection of Claims 10, 25-27, 30, 31, 38, 71 and 83 under 35 USC§103(a) over Petereit in view of Adams (US 6,139, 875)

The Examiner maintained the rejection of these claims, stating that the "rejection over Adams is maintained because the capsule shell of the present invention does not exclude the enteric coating layer which contains about 5% to about 50% stearyl alcohol as taught by Adams."

As discussed above, there is no teaching, suggestion, motivation or reason provided in Petereit for making a copolymer-containing composition that is substantially pH

independent, as currently claimed, and Adams fails to make up for this fundamental deficiency in Petereit.

The Examiner correctly states in the 9/20/07 Office Action that Adams “teaches an enteric composition.” Adams is directed to an enteric coating composition that “shows superior resistance to...simulated gastric fluid, while being readily broken down under the alkaline conditions which exist in the intestine.” (See Abstract). This is consistent with the Examiner’s characterization of Adams relating to enteric compositions. Adams describes an enteric coating composition which is “loaded with a combination of a solid flake material and hydrophobic aliphatic compound.” (col 2, lines 50-51). **Adams states, “(t)he present coating dissolves only at a pH above about 5.0”** (col. 5, lines 33-34), thereby clearly defining a pH level below which the enteric composition of Adams cannot dissolve. This is **exactly the opposite** of the dissolution properties of the claimed capsule shell and linker compositions of the present invention, which are pH independent.

There is no teaching, suggestion, motivation or reason provided in Adams for making a capsule shell or linker composition that is substantially pH independent, as currently claimed.

Therefore, one of ordinary skill in the art at the time the invention was made would have no reason, motivation, teaching or suggestion to combine the Petereit and Adams references in a way that would result in the claimed substantially pH independent composition of the present invention. These claims are not prima facie obvious, and withdrawal of the rejection of these claims over Petereit in view of Adams under 35 USC §103(a) is respectfully requested.

#### IV. Rejection of Claims 28, 29, 32-35 and 72 under 35 USC §103(a) over Petereit, Adams and Hatano

As discussed above, none of Petereit, Adams or Hatano, alone or in combination, provides any teaching, suggestion, motivation, or reason to one of ordinary skill in the art to combine these references to obtain a pH independent capsule shell or linker composition, and in fact, each of these references exemplifies the utility of the pH dependency of the various

copolymers recited in each of these references. These claims are not prima facie obvious, and withdrawal of the rejection of these claims over Petereit in view of Adams under 35 USC §103(a) is respectfully requested.

### **Conclusion**

The Examiner “recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention **where there is some teaching, suggestion or motivation to do so** found either in the references or in the knowledge generally available to one of ordinary skill in the art...The test for obviousness is not whether the features of the secondary references may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is **what the combined teachings** of the references would have suggested to those of ordinary skill in the art.”

Even with the combined teachings of the references discussed above, nothing therein would teach, suggest or motivate one of ordinary skill in the art to combine these teachings to obtain the presently claimed pH independent capsule shell and linker compositions. Each reference cited **makes use of and is dependent upon** the very pH dependence that the present Applicants were able to modify to create the new, useful and non-obvious pH independent capsule shell and linker compositions of the present invention. The cited references would therefore teach one of ordinary skill in the art directly **away from** changing the pH dependencies of the copolymers, since it is their very pH dependency that the cited references utilize to make the recited enteric compositions. The USPTO has therefore not made a prima facie case of obviousness for the present claims.

Reconsideration and withdrawal of the rejections based on 35 USC §112 and §103, and the prompt issuance of a Notice of Allowance, is respectfully requested. Should the Examiner have any questions or wish to discuss any aspect of this application, the Examiner is encouraged to call the undersigned attorney at the number below. If the

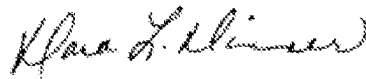
Serial No. 10/060,849  
Group Art Unit 1618

-32-

Examiner does not find the claims allowable, Applicants respectfully request an interview with the Examiner at the earliest opportunity.

It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Dara L. Dinner".

Dara L. Dinner  
Attorney for Applicants  
Registration No. 33,680

GLAXOSMITHKLINE  
Corporate Intellectual Property - UW2220  
P.O. Box 1539  
King of Prussia, PA 19406-0939  
Phone (610) 270-5017  
Facsimile (610) 270-5090